Amendments to the Claims

In accordance with 37 CFR § 1.121, please amend the claims and add new claims 26 – 50 as shown below.

1. (Currently amended) A cytotoxic reagent comprising an antibody and a moiety having ribonucleolytic activity derived from a non-human ribonuclease**, wherein said antibody and said moiety are linked through recombinant production**.

2. (Currently amended) A cytotoxic reagent comprising an internalizing antibody and a moiety having ribonucleolytic activity, wherein said internalizing antibody is directed against a lineage-dependent antigen or against an antigen associated with cancer cells**, and wherein said internalizing antibody and said moiety are linked through recombinant production**.

3. (Original) The cytotoxic reagent of claim 2 wherein the internalizing antibody is a monoclonal antibody.

4. (Original) The cytotoxic reagent of claim 3 wherein the monoclonal antibody is humanized or human.

5. (Original) The cytotoxic reagent of claim 4 wherein the antibody is a single chain antibody.

6. (Original) The cytotoxic reagent of claim 5 wherein said internalizing antibody is directed against an antigen selected from the group consisting of:

(a) B-cell antigens;

(b) T-cell antigens;

(c) Plasma cell antigens;

(d) HLA-DR lineage antigens;

(e) MUC1 antigens;

(f) EGP-1 antigens;

(g) EGP-2 antigens; and

(h) placental alkaline phosphatase antigen.

7. (Original) The cytotoxic reagent of claim 2 wherein said internalizing antibody is directed against a target antigen associated with a B- or T-cell lymphoma.

8. (Currently amended) The cytotoxic reagent of claim 7 wherein said antigen is an antigen selected from the group consisting of CD19, CD22, CD40, MUC1, ~~IL-15,~~ HLA-DR, EGP-1, EGP-2, and IL-15.

9. (Original) The cytotoxic reagent of claim 8 wherein said antigen is HLA-DR.

10. (Original) The cytotoxic reagent of claim of claim 2 wherein the internalizing antibody is LL1.

11. (Original) The cytotoxic reagent of claim of claim 8 wherein said antigen is CD22.

12. (Original) The cytotoxic reagent of claim 11 wherein the internalizing antibody is LL2.

13. (Original) The cytotoxic reagent of claim 8 wherein said antigen is MUC1.

14. (Original) The cytotoxic reagent of claim of claim 13 wherein the internalizing antibody is PAM4.

15. (Original) The cytotoxic reagent of claim 8 wherein said antigen is EGP-1.

16. (Original) The cytotoxic reagent of claim 15 wherein the internalizing antibody is RS7.

17. (Original) The cytotoxic reagent of claim 8 wherein said antigen is EGP-2.

18. (Original) The cytotoxic reagent of claim 17 wherein the internalizing antibody is RS11 or 17-1A.

19. (Original) The cytotoxic reagent of claim 2 wherein said internalizing antibody is a lineage-dependent antibody of a B-cell.

20. (Original) The cytotoxic reagent of claim 2 wherein said internalizing antibody is a lineage-dependent antibody of a T-cell.

21. (Original) The cytotoxic reagent of claim 2 wherein said internalizing antibody is a lineage-dependent antibody of a plasma cell.

22. (Original) The cytotoxic reagent of claim 2 wherein said antigen is CD22 or CD74.

23. (Original) The cytotoxic reagent of claim 2 wherein the internalizing antibody is LL1 or LL2.

24. (Original) A pharmaceutical composition comprising a cytotoxic reagent of claim 2 and a pharmaceutically acceptable carrier.

25. (Original) A method of killing cancer cells comprising administering to a subject in need thereof a pharmaceutical composition of claim 24.

26. (New) The cytotoxic reagent of claim 1 wherein said antibody is directed against an antigen selected from the group consisting of:

(a) B-cell antigens;

(b) T-cell antigens;

(c) Plasma cell antigens;

(d) HLA-DR lineage antigens;

(e) MUC1 antigens;

(f) EGP-1 antigens;

(g) EGP-2 antigens; and

(h) placental alkaline phosphatase antigen.

27. (New) The cytotoxic reagent of claim 1 wherein said antibody is associated with T-cells, myeloid cells, plasma cells or solid cancers.

28. (New) The cytotoxic reagent of claim 27 wherein said solid cancer is a cancer selected from the group consisting of neuroblastoma, malignant melanoma, breast, ovarian, prostate, lung, kidney and pancreas cancers.

29. (New) The cytotoxic reagent of claim 2 wherein said internalizing antibody is associated with T-cells, myeloid cells, plasma cells or solid cancers.

30. (New) The cytotoxic reagent of claim 29 wherein said solid cancer is a cancer selected from the group consisting of neuroblastoma, malignant melanoma, breast, ovarian, prostate, lung, kidney and pancreas cancers.

31. (New) The cytotoxic reagent of claim 2 wherein said internalizing antibody is directed to antigens selected from the group consisting of CD33, PSMA, PSA and PAP.

32. (New) The cytotoxic reagent of claim 2 wherein said internalizing antibody is selected from the group consisting of M195, G250 and RFB4.

33. (New) A pharmaceutical composition comprising a cytotoxic reagent of claim 1 and a pharmaceutically acceptable carrier.

34. (New) A method of killing cancer cells comprising administering to a subject in need thereof a pharmaceutical composition of claim 33.

35. (New) The method of claim 34 wherein said pharmaceutical composition is administered intranasal or by aerosol.

36. (New) The method of claim 34 wherein said pharmaceutical composition is administered via microspheres, liposomes or microparticles.

37. (New) The method of claim 25 wherein said pharmaceutical composition is administered intranasal or by aerosol.

38. (New) The method of claim 25 wherein said pharmaceutical composition is administered via microspheres, liposomes or microparticles.

39. (New) The method of claim 25 wherein said cancer cells are selected from the group of cancers consisting of lymphomas, melanomas, neuroblastomas and myelomas.

40. (New) The method of claim 39 wherein said internalizing antibody is directed to CD74.

41. (New) The method of claim 25 wherein said cancer cells are selected from the group consisting of breast, ovarian, prostate, lung, kidney, and pancreatic cancers, melanomas, neuroblastomas and myelomas.

42. (New) The method of claim 34 wherein said cancer cells are selected from the group consisting of breast, ovarian, prostate, lung, kidney, and pancreatic cancers, melanomas, neuroblastomas and myelomas.

43. (New) The method of claim 25 wherein said pharmaceutical composition is administered to said patient more than once.

44. (New) The method of claim 34 wherein said pharmaceutical composition is administered to said patient more than once.

45. (New) The method of claim 25 wherein 0.1 to about 1000 mg per day of said pharmaceutical composition is administered to said subject.

46. (New) The method of claim 34 wherein 0.1 to about 1000 mg per day of said pharmaceutical composition is administered to said subject.

47. (New) A method of selectively killing unwanted types of cells in a subject comprising administering to said subject a pharmaceutical composition of claim 24.

48. (New) A method of selectively killing unwanted types of cells in a subject comprising administering to said subject a pharmaceutical composition of claim 33.

49. (New) The method of claim 47 or 48 wherein said cells are involved in the development and progression of one or more autoimmune diseases.

50. (New) The method of claim 49 wherein said autoimmune diseases are selected from the group consisting of rheumatoid arthritis, systemic lupus erythematosis, immune thrombocytopenic purpura and Sjögren's syndrome.

51. (New) A cytotoxic reagent comprising an antibody and a moiety having ribonucleolytic activity derived from a non-human ribonuclease, wherein said antibody is directed against an antigen other than a B-cell antigen.

52. (New) A cytotoxic reagent comprising an internalizing antibody and a moiety having ribonucleolytic activity, wherein said internalizing antibody is directed against a lineage-dependent antigen or against an antigen associated with cancer cells, and wherein said internalizing antibody is directed against an antigen selected from the group consisting of:

a) T-cell antigens;

(b) MUC1 antigens;

(c) EGP-1 antigens;

(d) EGP-2 antigens; and

(e) placental alkaline phosphatase antigen.

53. (New) The cytotoxic reagent of claim 52 wherein the internalizing antibody is a monoclonal antibody.

54. (New) The cytotoxic reagent of claim 53 wherein the monoclonal antibody is humanized or human.

55. (New) The cytotoxic reagent of claim 54 wherein the antibody is a single chain antibody.

56. (New) The cytotoxic reagent of claim 52 wherein said internalizing antibody is directed against a target antigen associated with a T-cell lymphoma.

57. (New) The cytotoxic reagent of claim 52 wherein said antigen is an antigen selected from the group consisting of CD40, MUC1, EGP-1, EGP-2, and IL-15.

58. (New) The cytotoxic reagent of claim 57 wherein said antigen is IL-15.

59. (New) The cytotoxic reagent of claim 57 wherein said antigen is MUC1.

60. (New) The cytotoxic reagent of claim of claim 59 wherein the internalizing antibody is PAM4.

61. (New) The cytotoxic reagent of claim 57 wherein said antigen is EGP-1.

62. (New) The cytotoxic reagent of claim 61 wherein the internalizing antibody is RS7.

63. (New) The cytotoxic reagent of claim 57 wherein said antigen is EGP-2.

64. (New) The cytotoxic reagent of claim 63 wherein the internalizing antibody is RS11 or 17-1A.

65. (New) The cytotoxic reagent of claim 52 wherein said internalizing antibody is a lineage-dependent antibody of a T-cell.

66. (New) The cytotoxic reagent of claim 51 wherein said internalizing antibody is a vascular endothelium or angiogenesis receptor antibody.

67. (New) A pharmaceutical composition comprising a cytotoxic reagent of claim 52 and a pharmaceutically acceptable carrier.

68. (New) A method of killing cancer cells comprising administering to a subject in need thereof a pharmaceutical composition of claim 67.

69. (New) The cytotoxic reagent of claim 51 wherein said antibody is associated with T-cells or solid cancers.

70. (New) The cytotoxic reagent of claim 69 wherein said solid cancer is a cancer selected from the group consisting of neuroblastoma, malignant melanoma, breast, ovarian, prostate, lung, kidney and pancreas cancers.

71. (New) The cytotoxic reagent of claim 52 wherein said internalizing antibody is associated with T-cells or solid cancers.

72. (New) The cytotoxic reagent of claim 71 wherein said solid cancer is a cancer selected from the group consisting of neuroblastoma, malignant melanoma, breast, ovarian, prostate, lung, kidney and pancreas cancers.

73. (New) The cytotoxic reagent of claim 52 wherein said internalizing antibody is directed to antigens selected from the group consisting of PSMA, PSA and PAP.

74. (New) The cytotoxic reagent of claim 51 wherein said internalizing antibody is G250.

75. (New) A pharmaceutical composition comprising a cytotoxic reagent of claim 51 and a pharmaceutically acceptable carrier.

76. (New) A method of killing cancer cells comprising administering to a subject in need thereof a pharmaceutical composition of claim 75.

77. (New) The method of claim 76 wherein said pharmaceutical composition is administered intranasal or by aerosol.

78. (New) The method of claim 77 wherein said pharmaceutical composition is administered via microspheres, liposomes or microparticles.

79. (New) The method of claim 68 wherein said pharmaceutical composition is administered intranasal or by aerosol.

80. (New) The method of claim 79 wherein said pharmaceutical composition is administered via microspheres, liposomes or microparticles.

81. (New) The method of claim 68 wherein said cancer cells are selected from the group of cancers consisting of lymphomas, melanomas, neuroblastomas and myelomas.

82. (New) The method of claim 68 wherein said cancer cells are selected from the group consisting of breast, ovarian, prostate, lung, kidney, and pancreatic cancers, melanomas, neuroblastomas and myelomas.

83. (New) The method of claim 76 wherein said cancer cells are selected from the group consisting of breast, ovarian, prostate, lung, kidney, and pancreatic cancers, melanomas, neuroblastomas and myelomas.

84. (New) The method of claim 68 wherein said pharmaceutical composition is administered to said patient more than once.

85. (New) The method of claim 76 wherein said pharmaceutical composition is administered to said patient more than once.

86. (New) The method of claim 68 wherein 0.1 to about 1000 mg per day of said pharmaceutical composition is administered to said subject.

87. (New) The method of claim 76 wherein 0.1 to about 1000 mg per day of said pharmaceutical composition is administered to said subject.

88. (New) A method of selectively killing unwanted types of cells in a subject comprising administering to said subject a pharmaceutical composition of claim 67.

89. (New) A method of selectively killing unwanted types of cells in a subject comprising administering to said subject a pharmaceutical composition of claim 75.

90. (New) The method of claim 88 or 89 wherein said cells are involved in the development and progression of one or more autoimmune diseases.

91. (New) The method of claim 90 wherein autoimmune diseases are selected from the group consisting of rheumatoid arthritis, systemic lupus erythematosis, immune thrombocytopenic purpura and Sjögren's syndrome.

92. (New) A cytotoxic reagent comprising an antibody and a moiety having ribonucleolytic activity derived from a non-human ribonuclease, wherein said antibody is human or humanized.

93. (New) A cytotoxic reagent comprising an internalizing antibody and a moiety having ribonucleolytic activity, wherein said internalizing antibody is directed against a lineage-dependent antigen or against an antigen associated with cancer cells, and wherein said internalizing antibody is human or humanized.

94. (New) The cytotoxic reagent of claim 93 wherein the internalizing antibody is a monoclonal antibody.

95. (New) The cytotoxic reagent of claim 94 wherein the antibody is a single chain antibody.

96. (New) The cytotoxic reagent of claim 95 wherein said internalizing antibody is directed against an antigen selected from the group consisting of:

(a) B-cell antigens;

(b) T-cell antigens;

(c) Plasma cell antigens;

(d) HLA-DR lineage antigens;

(e) MUC1 antigens;

(f) EGP-1 antigens;

(g) EGP-2 antigens; and

(h) placental alkaline phosphatase antigen.

97. (New) The cytotoxic reagent of claim 93 wherein said internalizing antibody is directed against a target antigen associated with a B- or T-cell lymphoma.

98. (New) The cytotoxic reagent of claim 97 wherein said antigen is an antigen selected from the group consisting of CD19, CD22, CD40, MUC1, HLA-DR, EGP-1, EGP-2, and IL-15.

99. (New) The cytotoxic reagent of claim 98 wherein said antigen is HLA-DR.

100. (New) The cytotoxic reagent of claim of claim 93 wherein the internalizing antibody is LL1.

101. (New) The cytotoxic reagent of claim of claim 98 wherein said antigen is CD22.

102. (New) The cytotoxic reagent of claim 101 wherein the internalizing antibody is LL2.

103. (New) The cytotoxic reagent of claim 98 wherein said antigen is MUC1.

104. (New) The cytotoxic reagent of claim of claim 103 wherein the internalizing antibody is PAM4.

105. (New) The cytotoxic reagent of claim 98 wherein said antigen is EGP-1.

106. (New) The cytotoxic reagent of claim 105 wherein the internalizing antibody is RS7.

107. (New) The cytotoxic reagent of claim 98 wherein said antigen is EGP-2.

108. (New) The cytotoxic reagent of claim 107wherein the internalizing antibody is RS11 or 17-1A.

109. (New) The cytotoxic reagent of claim 93 wherein said internalizing antibody is a lineage-dependent antibody of a B-cell.

110. (New) The cytotoxic reagent of claim 93 wherein said internalizing antibody is a lineage-dependent antibody of a T-cell.

111. (New) The cytotoxic reagent of claim 93 wherein said internalizing antibody is a lineage-dependent antibody of a plasma cell.

112. (New) The cytotoxic reagent of claim 93 wherein said antigen is CD22 or CD74.

113. (New) The cytotoxic reagent of claim 93 wherein the internalizing antibody is LL1 or LL2.

114. (New) A pharmaceutical composition comprising a cytotoxic reagent of claim 93 and a pharmaceutically acceptable carrier.

115. (New) A method of killing cancer cells comprising administering to a subject in need thereof a pharmaceutical composition of claim 114.

116. (New) The cytotoxic reagent of claim 92 wherein said antibody is directed against an antigen selected from the group consisting of:

(a) B-cell antigens;

(b) T-cell antigens;

(c) Plasma cell antigens;

(d) HLA-DR lineage antigens;

(e) MUC1 antigens;

(f) EGP-1 antigens;

(g) EGP-2 antigens; and

(h) placental alkaline phosphatase antigen.

117. (New) The cytotoxic reagent of claim 92 wherein said antibody is associated with T-cells, myeloid cells, plasma cells or solid cancers.

118. (New) The cytotoxic reagent of claim 117 wherein said solid cancer is a cancer selected from the group consisting of neuroblastoma, malignant melanoma, breast, ovarian, prostate, lung, kidney and pancreas cancers.

119. (New) The cytotoxic reagent of claim 93 wherein said internalizing antibody is associated with T-cells, myeloid cells, plasma cells or solid cancers.

120. (New) The cytotoxic reagent of claim 119 wherein said solid cancer is a cancer selected from the group consisting of neuroblastoma, malignant melanoma, breast, ovarian, prostate, lung, kidney and pancreas cancers.

121. (New) The cytotoxic reagent of claim 93 wherein said internalizing antibody is directed to antigens selected from the group consisting of CD33, PSMA, PSA and PAP.

122. (New) The cytotoxic reagent of claim 93 wherein said internalizing antibody is selected from the group consisting of M195, G250 and RFB4.

123. (New) A pharmaceutical composition comprising a cytotoxic reagent of claim 92 and a pharmaceutically acceptable carrier.

124. (New) A method of killing cancer cells comprising administering to a subject in need thereof a pharmaceutical composition of claim 123.

125. (New) The method of claim 124 wherein said pharmaceutical composition is administered intranasal or by aerosol.

126. (New) The method of claim 125 wherein said pharmaceutical composition is administered via microspheres, liposomes or microparticles.

127. (New) The method of claim 115 wherein said pharmaceutical composition is administered intranasal or by aerosol.

128. (New) The method of claim 127 wherein said pharmaceutical composition is administered via microspheres, liposomes or microparticles.

129. (New) The method of claim 124 wherein said cancer cells are selected from the group of cancers consisting of lymphomas, melanomas, neuroblastomas and myelomas.

130. (New) The method of claim 129 wherein said internalizing antibody is directed to CD74.

131. (New) The method of claim 115 wherein said cancer cells are selected from the group consisting of breast, ovarian, prostate, lung, kidney, and pancreatic cancers, melanomas, neuroblastomas and myelomas.

132. (New) The method of claim 124 wherein said cancer cells are selected from the group consisting of breast, ovarian, prostate, lung, kidney, and pancreatic cancers, melanomas, neuroblastomas and myelomas.

133. (New) The method of claim 115 wherein said pharmaceutical composition is administered to said patient more than once.

134. (New) The method of claim 124 wherein said pharmaceutical composition is administered to said patient more than once.

135. (New) The method of claim 115 wherein 0.1 to about 1000 mg per day of said pharmaceutical composition is administered to said subject.

136. (New) The method of claim 124 wherein 0.1 to about 1000 mg per day of said pharmaceutical composition is administered to said subject.

137. (New) A method of selectively killing unwanted types of cells in a subject comprising administering to said subject a pharmaceutical composition of claim 114.

138. (New) A method of selectively killing unwanted types of cells in a subject comprising administering to said subject a pharmaceutical composition of claim 123.

139. (New) The method of claim 137 or 138 wherein said cells are involved in the development and progression of one or more autoimmune diseases.

140. (New) The method of claim 139 wherein said cells are involved in the development and progression of autoimmune diseases selected from the group consisting of rheumatoid arthritis, systemic lupus erythematosis, immune thrombocytopenic purpura and Sjögren's syndrome.

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